

**In the Claims**

1. (Currently amended) An isolated polypeptide, which polypeptide selected from the group consisting of:

- (i) has the amino acid sequence as recited in SEQ ID NO:2, SEQ ID NO:4, or a polypeptide comprising amino acid residues 373-503 of SEQ ID NO:6 and having adhesion molecule activity;
- (ii) a polypeptide comprising an amino acid sequence, wherein the amino acid sequence has greater than 95% sequence identity with amino acid residues 373-503 of SEQ ID NO:6, and wherein the polypeptide has adhesion molecule activity; and is a fragment thereof having activity as an adhesion molecule or having an antigenic determinant in common with the polypeptide of (i); or
- (iii) is a functional equivalent of a fragment of (i) or (ii) having adhesion molecule activity;

wherein the polypeptide or fragment contains a divalent metal ion bound to Ser378, Ser380 and Asp469, or equivalent residues.

2. (Withdrawn) A polypeptide which is a fragment according to claim 1(ii), which includes the adhesion molecule region, of the ADS1 polypeptide, said adhesion molecule region being defined as including between residues 250 and 365 inclusive of the amino acid sequence recited in SEQ ID NO:2, wherein said fragment possesses the catalytic residues SER258, SER260 and ASP348, or equivalent residues, and possesses adhesion molecule activity.

3. (Withdrawn) A polypeptide which is a functional equivalent according to claim 1(iii), is homologous to the amino acid sequence as recited in SEQ ID NO:2, possesses the catalytic residues SER258, SER260 and ASP348, or equivalent residues, and has adhesion molecule activity.

4. (Withdrawn) A polypeptide according to claim 3, wherein said functional equivalent is homologous to the adhesion molecule region of the ADS1 polypeptide.

5. (Withdrawn) A polypeptide which is a fragment according to claim 1(ii), which includes the adhesion molecule region of the ADS2 polypeptide, said adhesion molecule region being defined as including between residue 267 and residue 384 of the amino acid sequence

recited in SEQ ID NO:4, wherein said fragment possesses the catalytic residues SER273, SER275 and ASP365, or equivalent residues, and possesses adhesion molecule activity.

6. (Withdrawn) A polypeptide which is a functional equivalent according to claim 1(iii), is homologous to the amino acid sequence as recited in SEQ ID NO:4, possesses the catalytic residues SER273, SER275 and ASP365, or equivalent residues, and has adhesion molecule activity.

7. (Withdrawn) A polypeptide according to claim 6, wherein said functional equivalent is homologous to the adhesion molecule region of the ADS2 polypeptide.

8-10. (Cancelled)

11. (Currently amended) ~~A fragment or functional equivalent~~ The isolated polypeptide according to claim 1, which has greater than ~~[[30%]]~~ 95% sequence identity with ~~an amino acid sequence as recited in any one of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:6, or with a fragment thereof that possesses adhesion molecule activity,~~ as determined using BLAST version 2.3 using the default parameters specified by the National Center for Biotechnology Information, accessible at <http://www.ncbi.nlm.nih.gov/> and corresponding to Blosum 62 matrix; gap open penalty= 11 and gap extension penalty= 1.

12-18. (Cancelled)

19. (Currently amended) ~~The fragment of claim 11, wherein the fragment has~~ isolated polypeptide according to claim 1, which has greater than 98% sequence identity with an amino acid sequence as recited in any one of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:6.

20. (Currently amended) ~~The fragment of claim 11, wherein the fragment has~~ isolated polypeptide according to claim 1, which has greater than 99% sequence identity with an amino acid sequence as recited in any one of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:6.

21-23. (Cancelled)

24. (Withdrawn) A purified nucleic acid molecule which encodes a polypeptide according to claim 1.

25. (Withdrawn) A purified nucleic acid molecule according to claim 24, which has the nucleic acid sequence as recited in SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5, or is a redundant equivalent or fragment thereof.

26. (Withdrawn) A fragment of a purified nucleic acid molecule according to claim 24, which comprises between nucleotides 750 and 1095 of SEQ ED NO: 1, or is a redundant equivalent thereof.

27. (Withdrawn) A fragment of a purified nucleic acid molecule according to claim 24, which comprises between nucleotides 801 and 1152 of SEQ ID NO:3, or is a redundant equivalent thereof.

28. (Withdrawn) A fragment of a purified nucleic acid molecule according to claim 24, which comprises between nucleotides 1119 and 1509 of SEQ ID NO:5, or is a redundant equivalent thereof.

29. (Withdrawn) A purified nucleic acid molecule which hybridizes under high stringency conditions with a nucleic acid molecule according to claim 24.

30. (Withdrawn) A vector comprising a nucleic acid molecule as recited in claim 24.

31. (Withdrawn) A host cell transformed with a vector according to claim 30.

32. (Withdrawn) A ligand which binds specifically to, and which preferably inhibits the adhesion molecule activity of, a polypeptide according to claim 1.

33. (Withdrawn) A ligand according to claim 32, which is an antibody.

34. (Withdrawn) A compound that either increases or decreases the level of expression or activity of a polypeptide according to claim 1.

35. (Withdrawn) A compound that either increases or decreases the level of expression or activity of a polypeptide according to claim 1, wherein the compound binds to a polypeptide according to any one of claims 1 without inducing any of the biological effects of the polypeptide.

36. (Withdrawn) A compound that either increases or decreases the level of expression or activity of a polypeptide according to claim 1, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.

37. (Currently amended) ~~[[A]]~~ The isolated polypeptide according to ~~any one of claims 1~~ claim 1, an isolated nucleic acid molecule which encodes ~~[[a]]~~ the polypeptide according to claim 1, a vector comprising a nucleic acid molecule which encodes ~~[[a]]~~ the isolated polypeptide according to claim 1, a ligand which binds specifically to, and which ~~preferably~~ inhibits the adhesion molecule activity of, ~~[[a]]~~ the isolated polypeptide according to

claim 1, or a compound that either increases or decreases the level of expression or activity of [[a]] the isolated polypeptide according to claim 1, for use in therapy or diagnosis of disease.

38. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claim 1 or assessing the activity of a polypeptide according to any one of claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.

39. (Withdrawn) A method according to claim 38 that is carried out *in vitro*.

40. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claim 1 or assessing the activity of a polypeptide according to any one of claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, which comprises the steps of:

- (a) contacting a ligand which binds specifically to, and which preferably inhibits the adhesion molecule activity of, a polypeptide according to claim 1 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and
- (b) detecting said complex.

41. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claim 1 or assessing the activity of a polypeptide according to any one of claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, comprising the steps of:

- a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule which encodes a polypeptide according to claim 1 and the probe;
- b) contacting a control sample with said probe under the same conditions used in step a);and

- c) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease.

42. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claim 1 or assessing the activity of a polypeptide according to any one of claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, comprising:

- a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule which encodes a polypeptide according to claim 1 and the primer;
- b) contacting a control sample with said primer under the same conditions used in step a); and
- c) amplifying the sampled nucleic acid; and
- d) detecting the level of amplified nucleic acid from both patient and control samples;

wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

43. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claim 1 or assessing the activity of a polypeptide according to any one of claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease comprising:

- a) obtaining a tissue sample from a patient being tested for disease;
- b) isolating a nucleic acid molecule which encodes a polypeptide according to claim 1 from said tissue sample; and

- c) diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease.

44. (Withdrawn) The method of claim 43, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

45. (Withdrawn) The method of either claim 43, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridised portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and detecting the presence or absence of an unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

46. (Withdrawn) A method according to claim 38, wherein said disease is selected from cardiovascular diseases including atherosclerosis, ischaemia, restenosis, reperfusion injury, sepsis, haematological diseases such as leukaemia, blood clotting disorders, such as thrombosis, cancer including lung, prostate, breast, colorectal and brain tumours, metastasis, inflammatory diseases such as rhinitis, gastrointestinal diseases, including inflammatory bowel disease, ulcerative colitis, Crohn's disease, respiratory diseases including asthma, chronic obstructive pulmonary disease (COPD), respiratory distress syndrome, pulmonary fibrosis, immune disorders, including autoimmune diseases, rheumatoid arthritis, transplant rejection, allergy, liver diseases such as cirrhosis, endocrine diseases, such as diabetes, bone diseases such as osteoporosis, neurological diseases including stroke, multiple sclerosis, spinal cord injury, burns and wound healing, infections, preferably bacterial infection and most preferably E. coli infection.

47. (Withdrawn) A method of using a polypeptide according to claim 1 as an adhesion molecule.

48. (Withdrawn) A method of using a nucleic acid molecule according to claim 24 to express a protein that possesses adhesion molecule activity.

49. (Withdrawn) A method for effecting cell-cell adhesion, utilising a polypeptide according to claim 1.

50. (Currently amended) A pharmaceutical composition comprising [[a]] the isolated polypeptide according to claim 1, an isolated nucleic acid molecule which encodes [[a]] the polypeptide according to claim 1, a vector comprising a nucleic acid molecule which encodes [[a]] the isolated polypeptide according to claim 1, a ligand which binds specifically to, and which preferably inhibits the adhesion molecule activity of, [[a]] the isolated polypeptide according to claim 1, or a compound that either increases or decreases the level of expression or activity of [[a]] the isolated polypeptide according to claim 1, for use in therapy or diagnosis of disease.[[.]]

51. (Currently amended) A vaccine composition comprising [[a]] the isolated polypeptide according to claim 1 or a nucleic acid molecule which encodes [[a]] the isolated polypeptide according to claim 1.

52. (Currently amended) ~~A polypeptide according to claim 1, a nucleic acid molecule which encodes a polypeptide according to claim 1, a vector comprising a nucleic acid molecule which encodes a polypeptide according to claim 1, a ligand which binds specifically to, and which preferably inhibits the adhesion molecule activity of, a polypeptide according to claim 1, a compound that either increases or decreases the level of expression or activity of a polypeptide according to claim 1, or a pharmaceutical composition comprising one or more of the above for use in the manufacture of a medicament for the treatment of cardiovascular diseases including atherosclerosis, ischaemia, restenosis, reperfusion injury, sepsis, haematological diseases such as leukaemia, blood clotting disorders, such as thrombosis, cancer including lung, prostate, breast, colorectal and brain tumours, metastasis, A method of treating inflammatory diseases such as rhinitis, or gastrointestinal diseases, including inflammatory bowel disease, ulcerative colitis, Crohn's disease, respiratory diseases including asthma, chronic obstructive pulmonary disease (COPD), respiratory distress syndrome, pulmonary fibrosis, immune disorders, including autoimmune diseases, rheumatoid arthritis, transplant rejection, allergy, liver diseases such as cirrhosis, endocrine diseases, such as diabetes, bone diseases such as osteoporosis, neurological diseases including stroke, multiple sclerosis, spinal cord injury, burns and wound healing,~~

infections, preferably bacterial infection and most preferably E. coli infection comprising administering the pharmaceutical composition according to claim 50 to a subject in need thereof.

53. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a polypeptide according to claim 1, a nucleic acid molecule which encodes a polypeptide according to claim 1, a vector comprising a nucleic acid molecule which encodes a polypeptide according to claim 1, a ligand which binds specifically to, and which preferably inhibits the adhesion molecule activity of, a polypeptide according to claim 1, or a pharmaceutical composition comprising one or more of the above.

54. (Withdrawn) A method according to claim 53, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.

55. (Withdrawn) A method according to claim 53, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

56. (Withdrawn) A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to any one of claims 1, or the level of expression of a nucleic acid molecule which encodes a polypeptide according to claim 1 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.

57. (Withdrawn) A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 1, a nucleic acid molecule which encodes a polypeptide according to claim 1, or a host cell transformed with a vector comprising a nucleic acid molecule which encodes a polypeptide according to claim 1 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.



58. (Withdrawn) A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to claim 24; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.

59. (Withdrawn) The kit of claim 58, further comprising a third container holding an agent for digesting unhybridised RNA.

60. (Withdrawn) A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to any one of claims 24.

61. (Withdrawn) A kit comprising one or more antibodies that bind to a polypeptide as recited in claim 1 and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.

62. (Withdrawn) A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to claim 1.

63. (Withdrawn) A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 62 with a candidate compound and determining the effect of the compound on the disease of the animal.

64. (New) The method according to claim 52, wherein the inflammatory disease is rhinitis.

65. (New) The method according to claim 52, wherein the gastrointestinal disease is inflammatory bowel disease, ulcerative colitis or Crohn's disease.